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=> d his ful
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(FILE 'HOME' ENTERED AT 11:22:53 ON 13 OCT 2005)

FILE 'HCAPLUS' ENTERED AT 11:22:58 ON 13 OCT 2005 E US2004-786400/APPS

L1 1 SEA ABB=ON PLU=ON US2004-786400/AP

FILE 'REGISTRY' ENTERED AT 11:23:23 ON 13 OCT 2005

L2 46 SEA ABB=ON PLU=ON (10191-60-3/BI OR 103-71-9/BI OR 13623-94-4
/BI OR 145013-05-4/BI OR 1795-48-8/BI OR 214358-62-0/BI OR
2260-00-6/BI OR 24544-04-5/BI OR 2986-25-6/BI OR 298680-25-8/BI
OR 298680-26-9/BI OR 298680-27-0/BI OR 298680-28-1/BI OR
298680-29-2/BI OR 298680-30-5/BI OR 298680-31-6/BI OR 298680-32
-7/BI OR 298680-33-8/BI OR 298680-34-9/BI OR 298680-35-0/BI OR
298680-36-1/BI OR 298680-37-2/BI OR 298680-38-3/BI OR 298680-39
-4/BI OR 298680-40-7/BI OR 298680-41-8/BI OR 298680-42-9/BI OR
298680-43-0/BI OR 298680-44-1/BI OR 298680-45-2/BI OR 298680-46
-3/BI OR 298680-47-4/BI OR 298680-48-5/BI OR 298680-49-6/BI OR
298680-50-9/BI OR 3173-53-3/BI OR 5394-18-3/BI OR 574-98-1/BI
OR 61832-41-5/BI OR 62-56-6/BI OR 75-31-0/BI OR 75535-96-5/BI
OR 76536-66-8/BI OR 88-05-1/BI OR 9036-21-9/BI OR 95-53-4/BI)

L3 29 SEA ABB=ON PLU=ON L2 AND NCNC3/ESS

FILE 'HCAPLUS' ENTERED AT 11:24:11 ON 13 OCT 2005

1 SEA ABB=ON PLU=ON L1 AND L3

D IALL HITSTR

FILE 'REGISTRY' ENTERED AT 11:26:21 ON 13 OCT 2005

L5 STR

L4

L6 0 SEA SSS SAM L5

D QUE

L7 0 SEA SSS SAM L5

L8 14 SEA SSS FUL L5

FILE 'HCAPLUS' ENTERED AT 11:32:39 ON 13 OCT 2005
L9 2 SEA ABB=ON PLU=ON L8

FILE 'MEDLINE, EMBASE, BIOSIS, USPATFULL, USPAT2' ENTERED AT 11:33:04 ON 13 OCT 2005

L10 5 SEA ABB=ON PLU=ON L8

FILE 'HCAPLUS, USPATFULL, USPAT2' ENTERED AT 11:33:23 ON 13 OCT 2005
L11 6 DUP REM L9 L10 (1 DUPLICATE REMOVED)
ANSWERS '1-2' FROM FILE HCAPLUS
ANSWERS '3-6' FROM FILE USPATFULL

FILE 'BEILSTEIN' ENTERED AT 11:34:32 ON 13 OCT 2005 L12 0 SEA SSS FUL L5

FILE 'MARPAT' ENTERED AT 11:35:20 ON 13 OCT 2005

L13 0 SEA SSS SAM L5

L14 1 SEA SSS FUL L5

L15 0 SEA ABB=ON PLU=ON L14 NOT L9

FILE HOME

FILE HCAPLUS

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FILE COVERS 1907 - 13 Oct 2005 VOL 143 ISS 16 FILE LAST UPDATED: 12 Oct 2005 (20051012/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 12 OCT 2005 HIGHEST RN 865114-63-2 DICTIONARY FILE UPDATES: 12 OCT 2005 HIGHEST RN 865114-63-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE MEDLINE

FILE LAST UPDATED: 12 OCT 2005 (20051012/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP

RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/ http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE EMBASE

FILE COVERS 1974 TO 6 Oct 2005 (20051006/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS

FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 12 October 2005 (20051012/ED)

FILE RELOADED: 19 October 2003.

FILE USPATFULL

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 11 Oct 2005 (20051011/PD)
FILE LAST UPDATED: 11 Oct 2005 (20051011/ED)
HIGHEST GRANTED PATENT NUMBER: US6954941
HIGHEST APPLICATION PUBLICATION NUMBER: US2005223461

CA INDEXING IS CURRENT THROUGH 11 Oct 2005 (20051011/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 11 Oct 2005 (20051011/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2005

>>> the earliest to the latest publication.

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2005

```
USPAT2 is now available. USPATFULL contains full text of the
>>>
     original, i.e., the earliest published granted patents or
>>>
                                                                               <<<
     applications. USPAT2 contains full text of the latest US publications, starting in 2001, for the inventions covered in USPATFULL. A USPATFULL record contains not only the original
>>>
                                                                               <<<
>>>
>>>
                                                                               <<<
>>>
     published document but also a list of any subsequent
                                                                                <<<
     publications. The publication number, patent kind code, and
>>>
                                                                                <<<
     publication date for all the US publications for an invention
>>>
                                                                                <<<
     are displayed in the PI (Patent Information) field of USPATFULL
                                                                                <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc.
>>> USPATFULL and USPAT2 can be accessed and searched together
                                                                                <<<
     through the new cluster USPATALL. Type FILE USPATALL to
>>>
                                                                                <<<
>>> enter this cluster.
                                                                                <<<
>>>
                                                                                <<<
>>> Use USPATALL when searching terms such as patent assignees,
                                                                               <<<
>>> classifications, or claims, that may potentially change from
                                                                               <<<
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<<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE USPAT2

FILE COVERS 2001 TO PUBLICATION DATE: 13 Oct 2005 (20051013/PD)
FILE LAST UPDATED: 13 Oct 2005 (20051013/ED)
HIGHEST GRANTED PATENT NUMBER: US2005054189
HIGHEST APPLICATION PUBLICATION NUMBER: US2005229256
CA INDEXING IS CURRENT THROUGH 13 Oct 2005 (20051013/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 13 Oct 2005 (20051013/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2005

USPAT2 is a companion file to USPATFULL. USPAT2 contains full text of the latest US publications, starting in 2001, for the inventions covered in USPATFULL. USPATFULL contains full text of the original published US patents from 1971 to date and the original applications from 2001. In addition, a USPATFULL record for an invention contains a complete list of publications that may be searched in standard search fields, e.g., /PN, /PK, etc.

USPATFULL and USPAT2 can be accessed and searched together through the new cluster USPATALL. Type FILE USPATALL to enter this cluster.

Use USPATALL when searching terms such as patent assignees, classifications, or claims, that may potentially change from the earliest to the latest publication.

FILE BEILSTEIN
FILE LAST UPDATED ON OCTOBER 10, 2005

FILE COVERS 1771 TO 2005.
FILE CONTAINS 9,363,954 SUBSTANCES

>>>PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For mo detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

- \star please note that there are no formats free of cost.
- * SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE
- * ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE
- * ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.
- * FOR PRICE INFORMATION SEE HELP COST

NEW

* PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE

SEARCHED, SELECTED AND TRANSFERRED.

* NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.

FILE MARPAT

FILE CONTENT: 1988-PRESENT (VOL 143 ISS 15) (20051007/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES (COVERAGE TO THESE DATES IS NOT COMPLETE):

US 6916824 12 JUL 2005
DE 10359831 14 JUL 2005
EP 1550665 06 JUL 2005
JP 2005183717 07 JUL 2005
WO 2005079855 01 SEP 2005

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

CH~NO2

@27 28

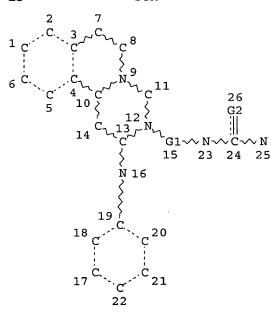
 $N \sim CN$

@29 30

 $N \sim NO2$

@31 32

=> d que stat ll1 L5 STR



REP G1=(1-5) C
VAR G2=O/27/29/NH/31
NODE ATTRIBUTES:
CONNECT IS E3 RC AT 13
CONNECT IS E2 RC AT 16
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE

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14 SEA FILE=REGISTRY SSS FUL L5
L8
             2 SEA FILE=HCAPLUS ABB=ON PLU=ON L8
L9
L10
             5 SEA L8
              6 DUP REM L9 L10 (1 DUPLICATE REMOVED)
L11
```

=> d l11 ibib abs hitstr 1-6 YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL' - CONTINUE? (Y)/N:y

L11 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:1006815 HCAPLUS

DOCUMENT NUMBER: 140:35974

TITLE: Treatment for depression and anxiety by the combination of a PDE IV inhibitor and an

antidepressant or an anxiolytic agent

Sobolov-Jaynes, Susan Beth; Schmidt, Christopher INVENTOR(S):

Joseph

PATENT ASSIGNEE(S): Pfizer Products Inc., USA PCT Int. Appl., 62 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION: DAMEDIM NO

PATENT NO.				KIND DATE			APPLICATION NO.					DATE					
WO	WO 2003105902				A1 20031224			1224	WO 2003-IB2295					20030605			
	W:	ΑE,	AG,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,
		ŪĠ,	US,	UΖ,	VN,	YU,	ZA,	ZM,	zw								
	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZM,	ZW,	AM,	ΑZ,	BY,
		KG,	ΚZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
US 2003235631				A1 20031225				US 2003-387060				20030312					
CA	CA 2488138				AA 20031224				CA 2003-2488138				20030605				
EP	EP 1517707			A1 20050330			EP 2003-727833				20030605						
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK	
BR 2003011903				A 20050607			BR 2003-11903				20030605						
PRIORITY APPLN. INFO.:								US 2002-389181P					P 20020617				
									,	WO 2	003-	IB22	95	1	W 20	0030	605

OTHER SOURCE(S): MARPAT 140:35974

The present invention relates to a method of treating depression or anxiety in a mammal, including a human, by administering to the mammal a PDE IV inhibitor in combination with an antidepressant or an anxiolytic agent. It also relates to pharmaceutical compns. containing a pharmaceutically acceptable carrier, a PDE IV inhibitor and an anxiolytic agent or antidepressant.

298680-25-8 IT

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment for depression and anxiety by combination of a PDE IV

inhibitor and an antidepressant or an anxiolytic agent)

298680-25-8 HCAPLUS RN

Urea, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-CN

trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

Me Me Me
$$CH_2-CH_2-NH-C-NH_2$$
 MeO N

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS 1 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2000:707163 HCAPLUS

DOCUMENT NUMBER:

133:266869

TITLE:

applicant 15 Preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-

ones as phosphodiesterase inhibitors. Oxford, Alexander William; Jack, David

PATENT ASSIGNEE(S):

Vanguard Medica Ltd., UK PCT Int. Appl., 77 pp.

INVENTOR(S): SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.				KIND DATE			APPLICATION NO.					DATE					
WO 2000058308			A1	1 20001005			WO 2000-GB1193					20000329					
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CR,
		CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,
		ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,	LU,
		LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,
		SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,
		ZW,	AM,	AZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM						
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZW,	AT,	BE,	CH,	CY,	DE,
		DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,
		CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG				
NZ 514158			A	20000329			NZ 2000-514158					20000329					
CA 2368413			AA	20001005			CA 2000-2368413					20000329					
AU 2000041274			A 5	20001016		AU 2000-41274					20000329						
AU 773504			B2	20040527													
ΕP	1165	558			A1		2002	0102		EP 2	000-	9208	57		2	0000	329
EP	1165	558			B1		2003	0924									

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO BR 2000009446 20020115 BR 2000-9446 20000329 Α JP 2002540207 T2 20021126 JP 2000-608010 20000329 AT 250602 Ε 20031015 AT 2000-920857 20000329 PT 1165558 Т 20040227 PT 2000-920857 20000329 ES 2208310 Т3 20040616 ES 2000-920857 20000329 20010926 US 2003036542 A1 20030220 US 2001-964260 B2 20040921 US 6794391 NO 2001004728 Α 20011123 NO 2001-4728 20010928 A1 20040902 US 2004-786650 20040224 US 2004171828 20040909 20040224 US 2004176353 **A1** US 2004-786400 GB 1999-7454 19990331 PRIORITY APPLN. INFO.: Α GB 1999-9802 A 19990428 WO 2000-GB1193 W 20000329 A3 20010926 US 2001-964260

OTHER SOURCE(S):

MARPAT 133:266869

GI

Title compds. [I; R1, R2 = alkyl, acyl; R5 = H, alkyl, alkenyl, alkynyl; R6 = H, alkyl, alkenyl, alkynyl, amino, alkylamino, dialkylamino, acylamino; R7, R8 = H, halo, OH, CF3, alkyl, alkenyl, alkynyl, acyl, alkythio, alkoxy, cycloalkyl; R9 = H, halo, OH, CF3, alkyl, alkenyl, alkynyl, acyl, alkythio, alkoxy, cycloalkyl; X = OCH2, CR3R4; R3, R4 = H, alkyl; R10, R11 = H, alkyl, cycloalkyl, Ph; Y = O, CHNO2, NCN, NH, NNO2; n = 2-4], were prepared I have a longer duration of action than the known compound trequinsin (9,10-dimethoxy-3-methyl-2-mesitylimino-2,3,6,7-tetrahydro-4H--pyrimido[6,1-a]isoquinolin-4-one) and do not have trequinsin's very bitter taste. Thus, Na cyanate was added dropwise to 9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(2-aminoethyl)-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one (preparation given) in aqueous HC1

I

at 80° followed by stirring for 2 h to give 54%
9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(N-carbamoyl-2-aminoethyl)3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one(II). II inhibited
PDE3 with IC50 = 0.46 µM and was tasteless.

IT 298680-25-8P 298680-26-9P 298680-27-0P 298680-28-1P 298680-29-2P 298680-30-5P

298680-31-6P 298680-32-7P 298680-33-8P 298680-34-9P 298680-35-0P 298680-36-1P 298680-37-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

RN 298680-25-8 HCAPLUS

CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH}-\text{C}-\text{NH}_2 \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-26-9 HCAPLUS

CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH-C-NHPr-i} \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-27-0 HCAPLUS

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-(methylamino)-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

Me Me Me NHMe NHMe
$$CH_2-CH_2-NH-C=CH-NO_2$$
 MeO MeO

RN 298680-28-1 HCAPLUS

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-[(1-methylethyl)amino]-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

RN 298680-29-2 HCAPLUS

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-[2-[[1-(dimethylamino)-2-nitroethenyl]amino]ethyl]-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

RN 298680-30-5 HCAPLUS

CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-phenyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH}-\text{C}-\text{NHPh} \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-31-6 HCAPLUS

CN Guanidine, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

Me Me Me NH
$$\frac{NH}{N}$$
 CH2-CH2-NH-C-NH2

RN 298680-32-7 HCAPLUS

CN Guanidine, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-nitro-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH}-\text{C}-\text{NH}-\text{NO}_2 \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-33-8 HCAPLUS

CN Urea, N-cyclohexyl-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

Me Me Me Me N
$$N - CH_2 - CH_2 - NH - C - NH$$
 MeO MeO

RN 298680-34-9 HCAPLUS

CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

MeO
$$\sim$$
 CH₂-CH₂-NH-C-NH₂ \sim MeO \sim MeO

RN 298680-35-0 HCAPLUS

CN Urea, [2-[2-[[2,6-bis(1-methylethyl)phenyl]imino]-6,7-dihydro-9,10-dimethoxy-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ i-pr & & & \\ N & & & \\ N & & & \\ MeO & & & \\ MeO & & & \\ \end{array}$$

RN 298680-36-1 HCAPLUS

CN Urea, [4-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]butyl]-(9CI) (CA INDEX NAME)

RN 298680-37-2 HCAPLUS

CN Guanidine, N-cyano-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N''-methyl- (9CI) (CA INDEX NAME)

Me Me NHMe NHMe
$$CH_2-CH_2-N=C-NH-CN$$

IT 298680-40-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

RN 298680-40-7 HCAPLUS

CN Carbamic acid, [[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]carbonimidoyl]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Me Me
$$t-BuO-C-NH$$
 O $CH_2-CH_2-N=C-NH-C-OBu-t$ MeO N

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 6 USPATFULL on STN

DUPLICATE 1

ACCESSION NUMBER:

2003:51584 USPATFULL

TITLE:
INVENTOR(S):

Derivatives of pyrimido[6.1-a]isoquinolin-4-one Oxford, Alexander William, Royston, UNITED KINGDOM

Jack, David, Wheathampstead, UNITED KINGDOM

		NUMBER	KIND	DATE	
PATENT INFORMATION:	US	2003036542	A1	20030220	
	US	6794391	B2	20040921	
APPLICATION INFO.:	US	2001-964260	A1	20010926	(9)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Dike, Bronstein, Roberts & Cushman, Intellectual

Property Patent Practice, EDWARDS & ANGELL, LLP, P.O.

Box 9169, Boston, MA, 02209

NUMBER OF CLAIMS: 50 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 5 Drawing Page(s)

LINE COUNT: 1581

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides compounds or salts thereof of the general formula

(I): ##STR1##

wherein each of R.sup.1 and RX independently represents a C.sub.1-6 alkyl or C.sub.2-7 acyl group; X represents OCH.sub.2 or a group CR.sup.3R.sup.4; wherein each of R.sup.3 or R.sup.4 independently represents a hydrogen atom or a C.sub.1-3 alkyl group; R.sup.5 represents a hydrogen atom or a C.sub.1-3 alkyl, C.sub.2-3 alkenyl or C.sub.2-3 alkynyl group; R.sup.6 represents a hydrogen atom or a C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, amino, C.sub.1-6alkylamino, di(C.sub.1-6) alkylamino or C.sub.2-7 acylamino group; each of R.sup.7 and R.sup.8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C.sub.1-6 alkyl,

C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.2-7 acyl, C.sub.1-6 alkylthio, C.sub.1-6 alkoxy, C.sub.3-6 cycloalkyl; and R.sup.9 represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.2-7 acyl, C.sub.1-6 alkylthio, C.sub.1-6 alkoxy or C.sub.3-6 cycloalkyl group. The compounds or salts thereof are useful for treatment of respiratory disorders such as asthma. Compounds of the invention have a longer duration of action than the known compound trequinsin (9,10-dimethoxy-3 methyl-2-mesitylimino-2,3,6,7-tetrahydro-.sub.4-H-pyrimido[6,1-a]isoquinolin-4-one).

RN 298680-26-9 USPATFULL
CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)

RN 298680-27-0 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-(methylamino)-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

Me Me NHMe NHMe
$$CH_2-CH_2-NH-C=CH-NO_2$$
 MeO N

RN 298680-28-1 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-[(1-methylethyl)amino]-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

RN 298680-29-2 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-[2-[[1-(dimethylamino)-2-nitroethenyl]amino]ethyl]-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

RN 298680-30-5 USPATFULL

CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-phenyl- (9CI) (CA INDEX NAME)

Me Me Me
$$CH_2-CH_2-NH-C-NHPh$$
 MeO N O N O MeO

RN 298680-31-6 USPATFULL

CN Guanidine, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

Me Me Me NH
$$\parallel$$
 CH2-CH2-NH-C-NH2 MeO MeO

RN 298680-32-7 USPATFULL

CN Guanidine, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-nitro-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2 - \text{CH}_2 - \text{NH} - \text{C} - \text{NH} - \text{NO}_2 \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-33-8 USPATFULL

CN Urea, N-cyclohexyl-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{N} \\ \text{CH}_2 - \text{CH}_2 - \text{NH} - \text{C} - \text{NH} \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-34-9 USPATFULL

CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

MeO
$$CH_2-CH_2-NH-C-NH_2$$

RN 298680-35-0 USPATFULL

RN 298680-36-1 USPATFULL

CN Urea, [4-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]butyl](9CI) (CA INDEX NAME)

Me Me Me
$$(CH_2)_4 - NH - C - NH_2$$
 MeO $(CH_2)_4 - NH - C - NH_2$

RN 298680-37-2 USPATFULL

CN Guanidine, N-cyano-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N''-methyl- (9CI) (CA INDEX NAME)

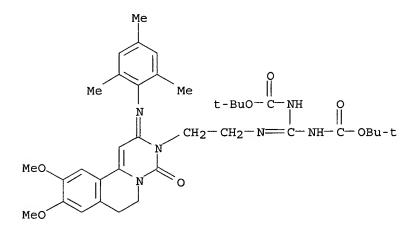
Me Me Me NHMe
$$CH_2-CH_2-N=C-NH-CN$$
 MeO N

IT 298680-40-7P

(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

RN 298680-40-7 USPATFULL

CN Carbamic acid, [[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)yl]ethyl]carbonimidoyl]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



L11 ANSWER 4 OF 6 USPATFULL on STN

ACCESSION NUMBER: 2004:227967 USPATFULL

TITLE: Derivatives of pyrimido[6,1-a]isoquinolin-4-one INVENTOR(S): Oxford, Alexander William, Royston, UNITED KINGDOM

Jack, David, Wheathampstead, UNITED KINGDOM

PATENT ASSIGNEE(S): Vernalis Limited (non-U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 2004176353 A1 20040909

APPLICATION INFO.: US 2004-786400 A1 20040224 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-964260, filed on 26 Sep

2001, PENDING

```
NUMBER
                                             DATE
                       GB 1999-7454
PRIORITY INFORMATION:
                                           19990331
                       GB 1999-9802
                                           19990428
                        WO 2000-58308
                                         20001005
DOCUMENT TYPE:
                        Utility
                        APPLICATION
FILE SEGMENT:
                        EDWARDS & ANGELL, LLP, P.O. BOX 55874, BOSTON, MA,
LEGAL REPRESENTATIVE:
                        02205
NUMBER OF CLAIMS:
                        50
EXEMPLARY CLAIM:
NUMBER OF DRAWINGS:
                       5 Drawing Page(s)
LINE COUNT:
                        1579
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Compounds of general formula (I) wherein each of R.sup.1 and R.sup.2
       independently represents a C.sub.1-6 alkyl or C.sub.2-7 acyl group;
       R.sup.5 represents a hydrogen atom or a C.sub.1-3 alkyl, C.sub.2-3
       alkenyl or C.sub.2-3 alkynyl group; R.sup.6 represents a hydrogen atom
       or a C.sub.1-6 alkyl C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, amino,
       C.sub.1-6 alkylamino, di(C.sub.1-6) alkylamino or C.sub.2-7 acylamino
       group; each of R.sup.7 and R.sup.8 independently represents a hydrogen
       or halogen atom or a hydroxy, trifluoromethyl, C.sub.1-6 alkyl,
       C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.2-7 acyl, C.sub.1-6
       alkythio, C.sub.3-6 alkoxy, C.sub.3-6 cycloalkyl; and R.sup.9 represents
       a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C.sub.1-6
       alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.1-7 acyl, C.sub.1-6
       alkythio. C.sub.1-6 alkoxy or C.sub.3-6 cycloalkyl group, X represents
       OCH.sub.2.sup.- or a group CR.sup.3R.sup.4, wherein each of R.sup.3 and
       R.sup.4 independently represents a hydrogen atom or a C.sub.1-3 alkyl
       group; each of R.sup.10 and R.sup.11 independently represents a hydrogen
       atom, a C.sub.1-3 alkyl C.sub.3-6 cycloalkyl or phenyl group; y
       represents an oxygen atom or a group CHNO.sub.2, NCN, NH or NNO.sub.2, n
       is an integer from 2 to 4; or a salt thereof; arm useful for treatment
       of respiratory disorders such as asthma. Compounds of the invention have
       a longer duration of action than the known compound trequinsin
       (9,10-dimethoxy-3-methyl-2-mesitylimino-2,3,6,7-tetrahydro-4H-pyrimido
       [6,1-a]isoquinolin-4-one) and do not have trequinsin's very bitter
       taste.
               ##STR1##
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    298680-25-8P 298680-26-9P 298680-27-0P
      298680-28-1P 298680-29-2P 298680-30-5P
      298680-31-6P 298680-32-7P 298680-33-8P
      298680-34-9P 298680-35-0P 298680-36-1P
      298680-37-2P
        (preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as
        phosphodiesterase inhibitors)
     298680-25-8 USPATFULL
RN
     Urea, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-
CN
```

trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-

(9CI) (CA INDEX NAME)

Me Me Me
$$CH_2-CH_2-NH-C-NH_2$$
 MeO N

RN 298680-26-9 USPATFULL

CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)

RN 298680-27-0 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-(methylamino)-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

Me Me NHMe NHMe
$$CH_2-CH_2-NH-C=CH-NO_2$$
 MeO MeO

RN 298680-28-1 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-[(1-methylethyl)amino]-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

RN 298680-29-2 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-[2-[[1-(dimethylamino)-2-nitroethenyl]amino]ethyl]-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

Me Me NMe NMe2
$$CH_2-CH_2-NH-C=CH-NO_2$$
 MeO MeO

RN 298680-30-5 USPATFULL

CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-phenyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2\text{-}\text{CH}_2\text{-}\text{NH-C-NHPh} \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-31-6 USPATFULL

CN Guanidine, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2 - \text{CH}_2 - \text{NH} - \text{C} - \text{NH}_2 \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-32-7 USPATFULL

CN Guanidine, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-nitro-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{NH} \\ \text{CH}_2\text{--}\text{CH}_2\text{--}\text{NH}\text{--}\text{C}\text{--}\text{NH}\text{--}\text{NO}_2 \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-33-8 USPATFULL

CN Urea, N-cyclohexyl-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl](9CI) (CA INDEX NAME)

Me Me Me Me Me
$$N \longrightarrow CH_2 - CH_2 - NH - C \longrightarrow NH \longrightarrow MeO$$

RN 298680-34-9 USPATFULL

CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

MeO
$$\sim$$
 CH₂-CH₂-NH-C-NH₂ \sim MeO \sim MeO

RN 298680-35-0 USPATFULL

CN Urea, [2-[2-[[2,6-bis(1-methylethyl)phenyl]imino]-6,7-dihydro-9,10-dimethoxy-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & & & & & & & & & & & \\ & & & & & & & & & & & & & \\ & & & & & & & & & & & \\ & & & & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & \\ &$$

RN 298680-36-1 USPATFULL

CN Urea, [4-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]butyl]-(9CI) (CA INDEX NAME)

Me Me Me
$$(CH_2)_4 - NH - C - NH_2$$

RN 298680-37-2 USPATFULL

CN Guanidine, N-cyano-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N''-methyl- (9CI) (CA INDEX NAME)

Me Me NHMe NHMe
$$CH_2-CH_2-N=C-NH-CN$$

IT 298680-40-7P

(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

RN 298680-40-7 USPATFULL

CN Carbamic acid, [[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]carbonimidoyl]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Me Me
$$t-BuO-C-NH$$
 O $CH_2-CH_2-N=C-NH-C-OBu-t$ MeO N O

L11 ANSWER 5 OF 6 USPATFULL on STN

ACCESSION NUMBER: 2004:222055 USPATFULL

TITLE: Derivatives of pyrimido[6,1-a]isoquinolin-4-one INVENTOR(S): Oxford, Alexander William, Royston, UNITED KINGDOM

Jack, David, Wheathampstead, UNITED KINGDOM

PATENT ASSIGNEE(S): Vernalis Limited (non-U.S. corporation)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-964260, filed on 26 Sep

2001, PENDING

PRIORITY INFORMATION: GB 1999-7454 19990331
GB 1999-9802 19990428

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Peter F. Corless, EDWARDS & ANGELL, LLP, P.O. Box 9169,

Boston, MA, 02209

NUMBER OF CLAIMS: 50 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 5 Drawing Page(s)

LINE COUNT: 1565

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Compounds of general formula (I) wherein each of R.sup.1 and R.sup.2 independently represents a C.sub.1-6 alkyl or C.sub.2-7 acyl group; R.sup.5 represents a hydrogen atom or a C.sub.1-3 alkyl, C.sub.2-3 alkenyl or C.sub.2-3 alkynyl group; R.sup.6 represents a hydrogen atom or a C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, amino, C.sub.1-6 alkylamino, di(C.sub.1-6) alkylamino or C.sub.2-7 acylamino group, each of R.sup.7 and R.sup.8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.2-7 acyl, C.sub.1-6 alkythio, C.sub.1-6 alkoxy, C.sub.3-6 cycloalkyl; and R.sup.9 represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.2-7 acyl, C.sub.1-6 alkythio, C.sub.1-6 alkoxy or C.sub.3-6 cycloalkyl group; X represents OCH.sub.2 or a group CR.sup.3R.sup.4, wherein each of R.sup.3 and

R.sup.4 independently represents a hydrogen atom or a C.sub.1-3 alkyl group; each of R.sup.10 and R.sup.11 independently represents a hydrogen atom, a C.sub.1-3 alkyl, C.sub.3-6 cycloalkyl or phenyl group; y represents an oxygen atom or a group CHNO.sub.2, NCN, NH or NNO.sub.2, n is an integer from 2 to 4; or a salt thereof; are useful for treatment of respiratory disorders such as asthma. Compounds of the invention have a longer duration of action than the known compound trequinsin (9,10-dimethoxy-3-methyl-2-mesitylimino-2,3,6,7-tetrahydro-4H-pyrimido[6,1-a]-isoquinolin-4-one) and do not have trequinsin's very bitter taste. ##STR1##

Me Me Me
$$CH_2-CH_2-NH-C-NH_2$$
 MeO N O MeO

RN 298680-26-9 USPATFULL
CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)

RN 298680-27-0 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3[2-[[1-(methylamino)-2-nitroethenyl]amino]ethyl]-2-[(2,4,6trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

Me Me NHMe NHMe
$$CH_2-CH_2-NH-C=CH-NO_2$$
 MeO MeO

RN 298680-28-1 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-[(1-methylethyl)amino]-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

RN 298680-29-2 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-[2-[[1-(dimethylamino)-2-nitroethenyl]amino]ethyl]-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

RN 298680-30-5 USPATFULL

CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-phenyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH}-\text{C-NHPh} \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-31-6 USPATFULL

CN Guanidine, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

Me Me Me NH
$$CH_2-CH_2-NH-C-NH_2$$
 MeO MeO

RN 298680-32-7 USPATFULL

CN Guanidine, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-nitro-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH}-\text{C-NH}-\text{NO}_2 \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-33-8 USPATFULL

CN Urea, N-cyclohexyl-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{N} \\ \text{CH}_2 - \text{CH}_2 - \text{NH} - \text{C} - \text{NH} \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-34-9 USPATFULL

CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

MeO
$$\sim$$
 CH₂-CH₂-NH-C-NH₂

RN 298680-35-0 USPATFULL

CN Urea, [2-[2-[[2,6-bis(1-methylethyl)phenyl]imino]-6,7-dihydro-9,10-dimethoxy-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

RN 298680-36-1 USPATFULL

CN Urea, [4-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]butyl]-(9CI) (CA INDEX NAME)

Me Me Me
$$(CH_2)_4 - NH - C - NH_2$$

RN 298680-37-2 USPATFULL

CN Guanidine, N-cyano-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N''-methyl- (9CI) (CA INDEX NAME)

Me Me Me NHMe
$$CH_2-CH_2-N=C-NH-CN$$
 MeO N

IT 298680-40-7P

(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

RN298680-40-7 USPATFULL

Carbamic acid, [[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-CN trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)yl]ethyl]carbonimidoyl]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Me Me
$$t-BuO-C-NH$$
 O $CH_2-CH_2-N=C-NH-C-OBu-t$ MeO MeO

L11 ANSWER 6 OF 6 USPATFULL on STN

ACCESSION NUMBER: 2003:334755 USPATFULL

TITLE:

Combination treatment for depression and anxiety

Sobolov-Jaynes, Susan B., Ivoryton, CT, UNITED STATES INVENTOR(S):

Schmidt, Christopher J., Old Lyme, CT, UNITED STATES

Pfizer Inc. (U.S. corporation) PATENT ASSIGNEE(S):

DATE NUMBER KIND PATENT INFORMATION: US 2003235631 20031225 **A**1 APPLICATION INFO.: US 2003-387060 **A1** 20030312 (10) NUMBER DATE

PRIORITY INFORMATION: US 2002-389181P 20020617 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49,

NEW YORK, NY, 10017-5612

NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
LINE COUNT: 1308

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to a method of treating depression or anxiety in a mammal, including a human, by administering to the mammal a PDE IV inhibitor in combination with an antidepressant or an anxiolytic agent. It also relates to pharmaceutical compositions containing a pharmaceutically acceptable carrier, a PDE IV inhibitor and an anxiolytic agent or antidepressant.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 298680-25-8

(treatment for depression and anxiety by combination of a PDE IV inhibitor and an antidepressant or an anxiolytic agent)

RN 298680-25-8 USPATFULL

CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

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=> d his ful
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(FILE 'HOME' ENTERED AT 11:22:53 ON 13 OCT 2005)

FILE 'HCAPLUS' ENTERED AT 11:22:58 ON 13 OCT 2005 E US2004-786400/APPS

L1 1 SEA ABB=ON PLU=ON US2004-786400/AP

FILE 'REGISTRY' ENTERED AT 11:23:23 ON 13 OCT 2005

L2 46 SEA ABB=ON PLU=ON (10191-60-3/BI OR 103-71-9/BI OR 13623-94-4
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2260-00-6/BI OR 24544-04-5/BI OR 2986-25-6/BI OR 298680-25-8/BI
OR 298680-26-9/BI OR 298680-27-0/BI OR 298680-28-1/BI OR
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OR 61832-41-5/BI OR 62-56-6/BI OR 75-31-0/BI OR 75535-96-5/BI
OR 76536-66-8/BI OR 88-05-1/BI OR 9036-21-9/BI OR 95-53-4/BI)

L3 29 SEA ABB=ON PLU=ON L2 AND NCNC3/ESS

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FILE 'REGISTRY' ENTERED AT 11:26:21 ON 13 OCT 2005

L5 STR

L4

L12

L6 0 SEA SSS SAM L5

D QUE

L7 0 SEA SSS SAM L5

L8 14 SEA SSS FUL L5

FILE 'HCAPLUS' ENTERED AT 11:32:39 ON 13 OCT 2005

L9 2 SEA ABB=ON PLU=ON L8

FILE 'MEDLINE, EMBASE, BIOSIS, USPATFULL, USPAT2' ENTERED AT 11:33:04 ON 13 OCT 2005

L10 5 SEA ABB=ON PLU=ON L8

FILE 'HCAPLUS, USPATFULL, USPAT2' ENTERED AT 11:33:23 ON 13 OCT 2005
L11 6 DUP REM L9 L10 (1 DUPLICATE REMOVED)
ANSWERS '1-2' FROM FILE HCAPLUS
ANSWERS '3-6' FROM FILE USPATFULL

FILE 'BEILSTEIN' ENTERED AT 11:34:32 ON 13 OCT 2005

FILE 'MARPAT' ENTERED AT 11:35:20 ON 13 OCT 2005

L13 0 SEA SSS SAM L5

L14 1 SEA SSS FUL L5

L15 0 SEA ABB=ON PLU=ON L14 NOT L9

0 SEA SSS FUL L5

FILE HOME

FILE HCAPLUS

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FILE COVERS 1907 - 13 Oct 2005 VOL 143 ISS 16 FILE LAST UPDATED: 12 Oct 2005 (20051012/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 12 OCT 2005 HIGHEST RN 865114-63-2 DICTIONARY FILE UPDATES: 12 OCT 2005 HIGHEST RN 865114-63-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE MEDLINE

FILE LAST UPDATED: 12 OCT 2005 (20051012/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP

RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/ http://www.nlm.nih.gov/pubs/techbull/nd04/nd04 mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE EMBASE

FILE COVERS 1974 TO 6 Oct 2005 (20051006/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS

FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 12 October 2005 (20051012/ED)

FILE RELOADED: 19 October 2003.

FILE USPATFULL

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 11 Oct 2005 (20051011/PD)

FILE LAST UPDATED: 11 Oct 2005 (20051011/ED)

>>> the earliest to the latest publication.

HIGHEST GRANTED PATENT NUMBER: US6954941

HIGHEST APPLICATION PUBLICATION NUMBER: US2005223461

CA INDEXING IS CURRENT THROUGH 11 Oct 2005 (20051011/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 11 Oct 2005 (20051011/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2005

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2005

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>>> USPAT2 is now available. USPATFULL contains full text of the
                                                                      <<<
>>> original, i.e., the earliest published granted patents or
                                                                      <<<
>>> applications. USPAT2 contains full text of the latest US
                                                                      <<<
>>> publications, starting in 2001, for the inventions covered in
                                                                      <<<
    USPATFULL. A USPATFULL record contains not only the original
>>>
                                                                      <<<
>>> published document but also a list of any subsequent
                                                                      <<<
>>> publications. The publication number, patent kind code, and
                                                                      <<<
>>> publication date for all the US publications for an invention
                                                                      <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL
                                                                      <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc.
                                                                      <<<
>>> USPATFULL and USPAT2 can be accessed and searched together
                                                                      <<<
    through the new cluster USPATALL. Type FILE USPATALL to
>>>
                                                                      <<<
>>> enter this cluster.
                                                                      <<<
                                                                      <<<
>>>
>>> Use USPATALL when searching terms such as patent assignees,
                                                                      <<<
>>> classifications, or claims, that may potentially change from
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This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE USPAT2

FILE COVERS 2001 TO PUBLICATION DATE: 13 Oct 2005 (20051013/PD)
FILE LAST UPDATED: 13 Oct 2005 (20051013/ED)
HIGHEST GRANTED PATENT NUMBER: US2005054189
HIGHEST APPLICATION PUBLICATION NUMBER: US2005229256
CA INDEXING IS CURRENT THROUGH 13 Oct 2005 (20051013/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 13 Oct 2005 (20051013/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2005

USPAT2 is a companion file to USPATFULL. USPAT2 contains full text of the latest US publications, starting in 2001, for the inventions covered in USPATFULL. USPATFULL contains full text of the original published US patents from 1971 to date and the original applications from 2001. In addition, a USPATFULL record for an invention contains a complete list of publications that may be searched in standard search fields, e.g., /PN, /PK, etc.

USPATFULL and USPAT2 can be accessed and searched together through the new cluster USPATALL. Type FILE USPATALL to enter this cluster.

Use USPATALL when searching terms such as patent assignees, classifications, or claims, that may potentially change from the earliest to the latest publication.

FILE BEILSTEIN
FILE LAST UPDATED ON OCTOBER 10, 2005

FILE COVERS 1771 TO 2005.
FILE CONTAINS 9,363,954 SUBSTANCES

>>>PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For mo detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

- * PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.
- * SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE
- * ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE
- * ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.
- * FOR PRICE INFORMATION SEE HELP COST

NEW

* PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE

Searched by Paul Schulwitz 571-272-2527

SEARCHED, SELECTED AND TRANSFERRED.

* NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.

FILE MARPAT

FILE CONTENT: 1988-PRESENT (VOL 143 ISS 15) (20051007/ED)

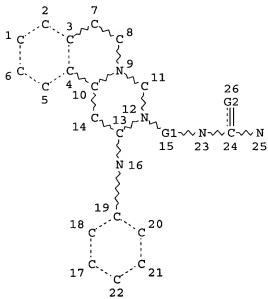
MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES (COVERAGE TO THESE DATES IS NOT COMPLETE):

6916824 12 JUL 2005 US 10359831 14 JUL 2005 DE 1550665 06 JUL 2005 EΡ JP 2005183717 07 JUL 2005 WO 2005079855 01 SEP 2005

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

=> d que stat 111 L5 STR



CH\sigma NO2 $N \sim CN$ $N \sim NO2$ @27 28 @29 30 @31 32

REP G1 = (1-5) C VAR G2=0/27/29/NH/31 NODE ATTRIBUTES: CONNECT IS E3 RC AT 13 CONNECT IS E2 RC AT 16 DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE

=> d l11 ibib abs hitstr 1-6
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL' - CONTINUE? (Y)/N:y

L11 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:1006815 HCAPLUS

DOCUMENT NUMBER: 140:35974

TITLE: Treatment for depression and anxiety by the combination of a PDE IV inhibitor and an

antidepressant or an anxiolytic agent

INVENTOR(S): Sobolov-Jaynes, Susan Beth; Schmidt, Christopher

Joseph

PATENT ASSIGNEE(S): Pfizer Products Inc., USA SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.					KIND DATE			j	APPL:	ICAT:	ION I	DATE					
WO	2003	1059	02		A1	_	2003	1224	1	WO 2	003-	IB22	95		2	0030	605
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		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,	UΑ,
		ŪĠ,	US,	UZ,	VN,	ΥU,	ZA,	ZM,	ZW								
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
		KG,	ΚZ,	MD,	RU,	TJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
		BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG
US	2003	2356	31		A1 20031225				1	US 20	003-	3870	50	20030312			
CA	2488	138			AA		2003	1224	(CA 2	003-2	2488	20030605				
EP	1517	707			A1 20050330				1	EP 20	003-	7278	33	20030605			
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙΤ,	LI,	LU,	NL,	SE,	MC,	PT,
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BR	2003	0119	03						BR 2003-11903					20030605			
PRIORITY	APP	LN.	INFO	. :					US 2002-389181P					P 20020617			
									1	WO 20	003-	IB22	95	1	W 20	0030	505

OTHER SOURCE(S): MARPAT 140:35974

AB The present invention relates to a method of treating depression or anxiety in a mammal, including a human, by administering to the mammal a PDE IV inhibitor in combination with an antidepressant or an anxiolytic agent. It also relates to pharmaceutical compns. containing a pharmaceutically acceptable carrier, a PDE IV inhibitor and an anxiolytic agent or antidepressant.

IT 298680-25-8

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment for depression and anxiety by combination of a PDE IV

inhibitor and an antidepressant or an anxiolytic agent)

298680-25-8 HCAPLUS RN

Urea, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-CN

trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH}-\text{C}-\text{NH}_2 \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2000:707163 HCAPLUS

DOCUMENT NUMBER:

133:266869

TITLE:

Preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-

ones as phosphodiesterase inhibitors. Oxford, Alexander William; Jack, David

PATENT ASSIGNEE(S):

Vanguard Medica Ltd., UK PCT Int. Appl., 77 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

INVENTOR(S):

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	CENT I	NO.			KIN	D 1	DATE		j	APPLICATION NO. DA					ATE		
						-											
WO	2000	0583	80		A 1		2000	1005	1	WO 2	000-0	GB11:	93		2	0000	329
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		CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,
		ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,	LU,
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	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY,	DE,
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CA	2368	413			AA	:	2000	1005	(CA 2	000-	2368	413		2	0000	329
ΑU	2000	0412	74		A5	:	2000	1016		AU 2	000-	4127	4		2	0000	329
AU	7735	04			B2	;	2004	0527									
ΕP	1165	558			A1	. :	2002	0102	:	EP 2	000-	9208	57		2	0000	329
ΕP	1165	558			B1	· ;	2003	0924									

applicants

	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GF	٤, :	ΙT,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	SI,	LT,	LV,	FI,	RO											
BR	2000	0094	46		A	:	2002	0115		BR	20	00-	9446			2	20000	329
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US	2003	03654	42		A1	:	2003	0220		US	20	01-	9642	60		2	20010	926
US	6794	391			B2	:	2004	0921										
NO	2001	0047	28		Α	:	2001	1123		NO	20	01-	4728			2	20010	928
US	2004	1718	28		A1	:	2004	0902		US	20	04-	7866	50		2	0040	224
US	2004	1763	53		A1	:	2004	0909		US	20	04-	7864	00		2	20040	224
PRIORITY	APP	LN.	INFO	. :						GB	19	99-	7454		1	A 1	9990	331
										GB	19	99-:	9802		1	A 1	9990	428
										WO	20	00-6	GB11	93	1	W 2	20000	329
										US	20	01-	9642	60	1	A3 2	20010	926

OTHER SOURCE(S):

MARPAT 133:266869

GΙ

Title compds. [I; R1, R2 = alkyl, acyl; R5 = H, alkyl, alkenyl, alkynyl; R6 = H, alkyl, alkenyl, alkynyl, amino, alkylamino, dialkylamino, acylamino; R7, R8 = H, halo, OH, CF3, alkyl, alkenyl, alkynyl, acyl, alkythio, alkoxy, cycloalkyl; R9 = H, halo, OH, CF3, alkyl, alkenyl, alkynyl, acyl, alkythio, alkoxy, cycloalkyl; X = OCH2, CR3R4; R3, R4 = H, alkyl; R10, R11 = H, alkyl, cycloalkyl, Ph; Y = O, CHNO2, NCN, NH, NNO2; n = 2-4], were prepared I have a longer duration of action than the known compound trequinsin (9,10-dimethoxy-3-methyl-2-mesitylimino-2,3,6,7-tetrahydro-4H--pyrimido[6,1-a]isoquinolin-4-one) and do not have trequinsin's very bitter taste. Thus, Na cyanate was added dropwise to 9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(2-aminoethyl)-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one (preparation given) in aqueous

Ι

HCl
 at 80° followed by stirring for 2 h to give 54%
 9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(N-carbamoyl-2-aminoethyl) 3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one(II). II inhibited
 PDE3 with IC50 = 0.46 μM and was tasteless.

IT 298680-25-8P 298680-26-9P 298680-27-0P 298680-28-1P 298680-29-2P 298680-30-5P

298680-31-6P 298680-32-7P 298680-33-8P 298680-34-9P 298680-35-0P 298680-36-1P 298680-37-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

RN 298680-25-8 HCAPLUS

CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl](9CI) (CA INDEX NAME)

Me Me Me
$$CH_2-CH_2-NH-C-NH_2$$
 MeO N

RN 298680-26-9 HCAPLUS

CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{Me} & \\ & \text{Me} & \\ & \text{N} & \\ & \text{CH}_2\text{--}\text{CH}_2\text{--}\text{NH--}\text{C--}\text{NHPr--}\text{i} \\ \\ & \text{MeO} & \\ & \text{MeO} & \\ & \text{MeO} & \\ \end{array}$$

RN 298680-27-0 HCAPLUS

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-(methylamino)-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

Me Me NHMe NHMe
$$CH_2-CH_2-NH-C=CH-NO_2$$
 MeO MeO

RN 298680-28-1 HCAPLUS

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-[(1-methylethyl)amino]-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

RN 298680-29-2 HCAPLUS

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-[2-[[1-(dimethylamino)-2-nitroethenyl]amino]ethyl]-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

RN 298680-30-5 HCAPLUS

Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-phenyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH}-\text{C}-\text{NHPh} \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-31-6 HCAPLUS

CN Guanidine, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

Me Me Me NH
$$\frac{NH}{N}$$
 CH2-CH2-NH-C-NH2

RN 298680-32-7 HCAPLUS

CN Guanidine, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-nitro-(9CI) (CA INDEX NAME)

RN 298680-33-8 HCAPLUS

CN Urea, N-cyclohexyl-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

Me Me Me Me N
$$\sim$$
 CH₂-CH₂-NH-C-NH- \sim MeO MeO

RN 298680-34-9 HCAPLUS

CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

RN 298680-35-0 HCAPLUS

CN Urea, [2-[2-[[2,6-bis(1-methylethyl)phenyl]imino]-6,7-dihydro-9,10-dimethoxy-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & & & & & & & & & & & \\ & & & & & & & & & & & & & \\ & & & & & & & & & & & \\ & & & & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & \\ &$$

RN 298680-36-1 HCAPLUS

CN Urea, [4-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]butyl]-(9CI) (CA INDEX NAME)

Me Me
$$(CH_2)_4-NH-C-NH_2$$
 MeO N

RN 298680-37-2 HCAPLUS

CN Guanidine, N-cyano-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N''-methyl- (9CI) (CA INDEX NAME)

Me Me NHMe NHMe
$$CH_2-CH_2-N=C-NH-CN$$

IT 298680-40-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

RN 298680-40-7 HCAPLUS

CN Carbamic acid, [[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H) yl]ethyl]carbonimidoyl]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Me
$$t-BuO-C-NH$$
 O $CH_2-CH_2-N=C-NH-C-OBu-t$

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS 1 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 6 USPATFULL on STN DUPLICATE 1

ACCESSION NUMBER:

2003:51584 USPATFULL

TITLE: INVENTOR(S): Derivatives of pyrimido[6.1-a]isoquinolin-4-one Oxford, Alexander William, Royston, UNITED KINGDOM

Jack, David, Wheathampstead, UNITED KINGDOM

	 NUMBER	KIND	DATE	
PATENT INFORMATION:	 2003036542 6794391	A1 B2	20030220	
APPLICATION INFO.:	 2001-964260	A1	20010926	(9)

		NUMBER	DATE
PRIORITY I	010.111101 0-	1999-7454 1999-9802	19990331 19990428

DOCUMENT TYPE: FILE SEGMENT:

Utility APPLICATION

LEGAL REPRESENTATIVE:

Dike, Bronstein, Roberts & Cushman, Intellectual

Property Patent Practice, EDWARDS & ANGELL, LLP, P.O.

Box 9169, Boston, MA, 02209

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

50 1

NUMBER OF DRAWINGS:

5 Drawing Page(s)

LINE COUNT:

1581

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention provides compounds or salts thereof of the general formula AB

##STR1## (I):

wherein each of R.sup.1 and RX independently represents a C.sub.1-6 alkyl or C.sub.2-7 acyl group; X represents OCH.sub.2 or a group CR.sup.3R.sup.4; wherein each of R.sup.3 or R.sup.4 independently represents a hydrogen atom or a C.sub.1-3 alkyl group; R.sup.5 represents a hydrogen atom or a C.sub.1-3 alkyl, C.sub.2-3 alkenyl or C.sub.2-3 alkynyl group; R.sup.6 represents a hydrogen atom or a C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, amino, C.sub.1-6alkylamino, di(C.sub.1-6) alkylamino or C.sub.2-7 acylamino group; each of R.sup.7 and R.sup.8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C.sub.1-6 alkyl,

C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.2-7 acyl, C.sub.1-6 alkylthio, C.sub.1-6 alkoxy, C.sub.3-6 cycloalkyl; and R.sup.9 represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.2-7 acyl, C.sub.1-6 alkylthio, C.sub.1-6 alkoxy or C.sub.3-6 cycloalkyl group. The compounds or salts thereof are useful for treatment of respiratory disorders such as asthma. Compounds of the invention have a longer duration of action than the known compound trequinsin (9,10-dimethoxy-3 methyl-2-mesitylimino-2,3,6,7-tetrahydro-.sub.4-H-pyrimido[6,1-a]isoquinolin-4-one).

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH}-\text{C}-\text{NH}_2 \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-26-9 USPATFULL
CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH-C-NHPr-i} \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-27-0 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-(methylamino)-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

Me Me NHMe NHMe
$$CH_2-CH_2-NH-C=CH-NO_2$$
 MeO MeO

RN 298680-28-1 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-[(1-methylethyl)amino]-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

RN 298680-29-2 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-[2-[[1-(dimethylamino)-2-nitroethenyl]amino]ethyl]-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

Me Me NMe2 NMe2
$$CH_2-CH_2-NH-C=CH-NO_2$$
 MeO MeO

RN 298680-30-5 USPATFULL

CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-phenyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH}-\text{C-NHPh} \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-31-6 USPATFULL CN Guanidine, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

RN 298680-32-7 USPATFULL
CN Guanidine, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-nitro- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH}-\text{C}-\text{NH}-\text{NO}_2 \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-33-8 USPATFULL

CN Urea, N-cyclohexyl-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

Me Me Me Me Me
$$N \longrightarrow CH_2 - CH_2 - NH \longrightarrow C \longrightarrow NH$$

RN 298680-34-9 USPATFULL

CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

MeO
$$\sim$$
 CH₂-CH₂-NH-C-NH₂

RN 298680-35-0 USPATFULL

CN Urea, [2-[2-[[2,6-bis(1-methylethyl)phenyl]imino]-6,7-dihydro-9,10-dimethoxy-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & i \text{-Pr} & & & \\ & N & & \\ & N & & \\ & CH_2 - CH_2 - NH - C - NH_2 \\ & & \\ & MeO & & \\$$

RN 298680-36-1 USPATFULL

CN Urea, [4-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]butyl]-(9CI) (CA INDEX NAME)

Me Me Me
$$(CH_2)_4-NH-C-NH_2$$
 MeO $(CH_2)_4-NH-C-NH_2$

RN 298680-37-2 USPATFULL

CN Guanidine, N-cyano-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N''-methyl- (9CI) (CA INDEX NAME)

Me Me NHMe NHMe
$$CH_2-CH_2-N=C-NH-CN$$

IT 298680-40-7P

(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

RN 298680-40-7 USPATFULL

CN Carbamic acid, [[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]carbonimidoyl]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Me Me
$$t-BuO-C-NH$$
 O $t-BuO-C-NH-C-OBu-t$ MeO $t-BuO-C-NH-C-OBu-t$

L11 ANSWER 4 OF 6 USPATFULL on STN

ACCESSION NUMBER: 2004:227967 USPATFULL

TITLE: Derivatives of pyrimido[6,1-a]isoquinolin-4-one

INVENTOR(S): Oxford, Alexander William, Royston, UNITED KINGDOM

Jack, David, Wheathampstead, UNITED KINGDOM

PATENT ASSIGNEE(S): Vernalis Limited (non-U.S. corporation)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-964260, filed on 26 Sep

2001, PENDING

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NUMBER
                                            DATE
                         -----
PRIORITY INFORMATION:
                       GB 1999-7454
                                          19990331
                       GB 1999-9802
                                          19990428
                       WO 2000-58308
                                           20001005
DOCUMENT TYPE:
                       Utility
FILE SEGMENT:
                       APPLICATION
LEGAL REPRESENTATIVE:
                       EDWARDS & ANGELL, LLP, P.O. BOX 55874, BOSTON, MA,
                       02205
NUMBER OF CLAIMS:
                       50
EXEMPLARY CLAIM:
                       1
NUMBER OF DRAWINGS:
                       5 Drawing Page(s)
LINE COUNT:
                       1579
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Compounds of general formula (I) wherein each of R.sup.1 and R.sup.2
       independently represents a C.sub.1-6 alkyl or C.sub.2-7 acyl group;
       R.sup.5 represents a hydrogen atom or a C.sub.1-3 alkyl, C.sub.2-3
       alkenyl or C.sub.2-3 alkynyl group; R.sup.6 represents a hydrogen atom
       or a C.sub.1-6 alkyl C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, amino,
       C.sub.1-6 alkylamino, di(C.sub.1-6) alkylamino or C.sub.2-7 acylamino
       group; each of R.sup.7 and R.sup.8 independently represents a hydrogen
       or halogen atom or a hydroxy, trifluoromethyl, C.sub.1-6 alkyl,
       C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.2-7 acyl, C.sub.1-6
       alkythio, C.sub.3-6 alkoxy, C.sub.3-6 cycloalkyl; and R.sup.9 represents
       a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C.sub.1-6
       alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.1-7 acyl, C.sub.1-6
       alkythio. C.sub.1-6 alkoxy or C.sub.3-6 cycloalkyl group, X represents
       OCH.sub.2.sup.- or a group CR.sup.3R.sup.4, wherein each of R.sup.3 and
       R.sup.4 independently represents a hydrogen atom or a C.sub.1-3 alkyl
       group; each of R.sup.10 and R.sup.11 independently represents a hydrogen
       atom, a C.sub.1-3 alkyl C.sub.3-6 cycloalkyl or phenyl group; y
       represents an oxygen atom or a group CHNO.sub.2, NCN, NH or NNO.sub.2, n
       is an integer from 2 to 4; or a salt thereof; arm useful for treatment
       of respiratory disorders such as asthma: Compounds of the invention have
       a longer duration of action than the known compound trequinsin
       (9,10-dimethoxy-3-methyl-2-mesitylimino-2,3,6,7-tetrahydro-4H-pyrimido
       [6,1-a]isoquinolin-4-one) and do not have trequinsin's very bitter
       taste.
               ##STR1##
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 298680-25-8P 298680-26-9P 298680-27-0P
      298680-28-1P 298680-29-2P 298680-30-5P
      298680-31-6P 298680-32-7P 298680-33-8P
      298680-34-9P 298680-35-0P 298680-36-1P
      298680-37-2P
        (preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as
        phosphodiesterase inhibitors)
     298680-25-8 USPATFULL
RN
CN
     Urea, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-
```

trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-

(9CI) (CA INDEX NAME)

Me Me Me
$$CH_2-CH_2-NH-C-NH_2$$
 MeO N

RN 298680-26-9 USPATFULL

CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{Me} & \\ & \text{Me} & \\ & \text{N} & \\ & \text{CH}_2\text{--}\text{CH}_2\text{--}\text{NH--}\text{C--}\text{NHPr--}\text{i} \\ & \text{MeO} & \\ & \text{MeO} & \\ & \text{N} & \text{O} \end{array}$$

RN 298680-27-0 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-(methylamino)-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

Me Me NHMe NHMe
$$CH_2-CH_2-NH-C=CH-NO_2$$
 MeO MeO

RN 298680-28-1 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-[(1-methylethyl)amino]-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

RN 298680-29-2 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-[2-[[1-(dimethylamino)-2-nitroethenyl]amino]ethyl]-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

Me Me NMe NMe2
$$CH_2-CH_2-NH-C$$
 $CH-NO_2$ CH_2-CH_2-NH-C

RN 298680-30-5 USPATFULL

CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-phenyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2\text{--}\text{CH}_2\text{--}\text{NH--}\text{C--}\text{NHPh} \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-31-6 USPATFULL

CN Guanidine, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

Me Me Me NH
$$\frac{NH}{N}$$
 CH2-CH2-NH-C-NH2

RN 298680-32-7 USPATFULL
CN Guanidine, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-nitro-(9CI) (CA INDEX NAME)

RN 298680-33-8 USPATFULL
CN Urea, N-cyclohexyl-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl](9CI) (CA INDEX NAME)

Me Me Me Me N
$$CH_2 - CH_2 - NH - C - NH$$
 MeO MeO

RN 298680-34-9 USPATFULL

CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

RN 298680-35-0 USPATFULL

CN Urea, [2-[2-[[2,6-bis(1-methylethyl)phenyl]imino]-6,7-dihydro-9,10-dimethoxy-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} i \text{-Pr} & & \\ \hline \\ N & \\ CH_2 - CH_2 - NH - C - NH_2 \\ \hline \\ MeO & \\ \end{array}$$

RN 298680-36-1 USPATFULL

CN Urea, [4-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]butyl]-(9CI) (CA INDEX NAME)

RN 298680-37-2 USPATFULL

CN Guanidine, N-cyano-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N''-methyl- (9CI) (CA INDEX NAME)

Me Me NHMe NHMe
$$CH_2-CH_2-N=C-NH-CN$$
 MeO MeO

IT 298680-40-7P

(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

RN 298680-40-7 USPATFULL

CN Carbamic acid, [[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]carbonimidoyl]bis-, bis(1,1-dimethylethyl) ester (9CI) (CFINDEX NAME)

Me Me
$$t-BuO-C-NH$$
 O $CH_2-CH_2-N=C-NH-C-OBu-t$ MeO N O

L11 ANSWER 5 OF 6 USPATFULL on STN

ACCESSION NUMBER: 2004:222055 USPATFULL

TITLE: Derivatives of pyrimido[6,1-a]isoquinolin-4-one INVENTOR(S): Oxford, Alexander William, Royston, UNITED KINGDOM

Jack, David, Wheathampstead, UNITED KINGDOM

PATENT ASSIGNEE(S): Vernalis Limited (non-U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 2004171828 A1 20040902

APPLICATION INFO: US 2004-786650 A1 20040224 (10)

PELATED APPLIA INFO: Division of Ser No. US 2001-964260 file

RELATED APPLN. INFO.: Division of Ser. No. US 2001-964260, filed on 26 Sep

2001, PENDING

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Peter F. Corless, EDWARDS & ANGELL, LLP, P.O. Box 9169,

Boston, MA, 02209

NUMBER OF CLAIMS: 50 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 5 Drawing Page(s)

LINE COUNT: 1565

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Compounds of general formula (I) wherein each of R.sup.1 and R.sup.2 independently represents a C.sub.1-6 alkyl or C.sub.2-7 acyl group; R.sup.5 represents a hydrogen atom or a C.sub.1-3 alkyl, C.sub.2-3 alkenyl or C.sub.2-3 alkynyl group; R.sup.6 represents a hydrogen atom or a C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, amino, C.sub.1-6 alkylamino, di(C.sub.1-6) alkylamino or C.sub.2-7 acylamino group, each of R.sup.7 and R.sup.8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.2-7 acyl, C.sub.1-6 alkythio, C.sub.1-6 alkoxy, C.sub.3-6 cycloalkyl; and R.sup.9 represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C.sub.1-6 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkynyl, C.sub.2-7 acyl, C.sub.1-6 alkythio, C.sub.1-6 alkoxy or C.sub.3-6 cycloalkyl group; X represents OCH.sub.2 or a group CR.sup.3R.sup.4, wherein each of R.sup.3 and

R.sup.4 independently represents a hydrogen atom or a C.sub.1-3 alkyl group; each of R.sup.10 and R.sup.11 independently represents a hydrogen atom, a C.sub.1-3 alkyl, C.sub.3-6 cycloalkyl or phenyl group; y represents an oxygen atom or a group CHNO.sub.2, NCN, NH or NNO.sub.2, n is an integer from 2 to 4; or a salt thereof; are useful for treatment of respiratory disorders such as asthma. Compounds of the invention have a longer duration of action than the known compound trequinsin (9,10-dimethoxy-3-methyl-2-mesitylimino-2,3,6,7-tetrahydro-4H-pyrimido[6,1-a]-isoquinolin-4-one) and do not have trequinsin's very bitter taste. ##STR1##

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH}-\text{C}-\text{NH}_2 \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-26-9 USPATFULL
CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-(1-methylethyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2-\text{CH}_2-\text{NH}-\text{C}-\text{NHPr-i} \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-27-0 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-(methylamino)-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

Me Me NHMe NHMe
$$CH_2-CH_2-NH-C=CH-NO_2$$
 MeO MeO

RN 298680-28-1 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 2,3,6,7-tetrahydro-9,10-dimethoxy-3-[2-[[1-[(1-methylethyl)amino]-2-nitroethenyl]amino]ethyl]-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

RN 298680-29-2 USPATFULL

CN 4H-Pyrimido[6,1-a]isoquinolin-4-one, 3-[2-[[1-(dimethylamino)-2-nitroethenyl]amino]ethyl]-2,3,6,7-tetrahydro-9,10-dimethoxy-2-[(2,4,6-trimethylphenyl)imino]- (9CI) (CA INDEX NAME)

Me Me NMe2 NMe2
$$CH_2-CH_2-NH-C=CH-NO_2$$
 MeO MeO

RN 298680-30-5 USPATFULL

CN Urea, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-phenyl- (9CI) (CA INDEX NAME)

Me Me Me
$$CH_2-CH_2-NH-C-NHPh$$
 MeO N

RN 298680-31-6 USPATFULL

CN Guanidine, [2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

Me Me Me NH
$$\parallel$$
 CH₂-CH₂-NH-C-NH₂ MeO MeO

RN 298680-32-7 USPATFULL

CN Guanidine, N-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N'-nitro-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{NH} \\ \text{CH}_2-\text{CH}_2-\text{NH}-\text{C-NH}-\text{NO}_2 \\ \\ \text{MeO} \\ \text{MeO} \\ \end{array}$$

RN 298680-33-8 USPATFULL

CN Urea, N-cyclohexyl-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-(9CI) (CA INDEX NAME)

Me Me Me N
$$CH_2-CH_2-NH-C-NH$$
 MeO MeO

RN 298680-34-9 USPATFULL

CN Urea, [2-[6,7-dihydro-9,10-dimethoxy-2-[(2-methylphenyl)imino]-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

MeO
$$\sim$$
 CH₂-CH₂-NH-C-NH₂ \sim MeO \sim MeO

RN 298680-35-0 USPATFULL

CN Urea, [2-[2-[[2,6-bis(1-methylethyl)phenyl]imino]-6,7-dihydro-9,10-dimethoxy-4-oxo-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ &$$

RN 298680-36-1 USPATFULL

CN Urea, [4-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]butyl]-(9CI) (CA INDEX NAME)

Me Me Me
$$(CH_2)_4-NH-C-NH_2$$
 MeO $(CH_2)_4-NH-C-NH_2$

RN 298680-37-2 USPATFULL

CN Guanidine, N-cyano-N'-[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-trimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)-yl]ethyl]-N''-methyl- (9CI) (CA INDEX NAME)

Me Me NHMe NHMe
$$CH_2-CH_2-N=C-NH-CN$$
 MeO N

298680-40-7P IT

(preparation of 2-aryliminopyrimido[6,1-a]isoquinolin-4-ones as phosphodiesterase inhibitors)

RN 298680-40-7 USPATFULL

Carbamic acid, [[2-[6,7-dihydro-9,10-dimethoxy-4-oxo-2-[(2,4,6-CNtrimethylphenyl)imino]-2H-pyrimido[6,1-a]isoquinolin-3(4H)yl]ethyl]carbonimidoyl]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA. INDEX NAME)

Me Me
$$t-BuO-C-NH$$
 O $CH_2-CH_2-N=C-NH-C-OBu-t$ MeO N

L11 ANSWER 6 OF 6 USPATFULL on STN

ACCESSION NUMBER:

2003:334755 USPATFULL

TITLE:

INVENTOR(S):

Combination treatment for depression and anxiety Sobolov-Jaynes, Susan B., Ivoryton, CT, UNITED STATES Schmidt, Christopher J., Old Lyme, CT, UNITED STATES

Pfizer Inc. (U.S. corporation) PATENT ASSIGNEE(S):

	NUMBER	KIND	DATE	
PATENT INFORMATION: APPLICATION INFO.:	US 2003235631 US 2003-387060	A1 A1	20031225 20030312	(10)
	NUMBER	DA	TE	

PRIORITY INFORMATION: US 2002-389181P 20020617 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49,

NEW YORK, NY, 10017-5612

NUMBER OF CLAIMS: 11 EXEMPLARY CLAIM: 1 LINE COUNT: 1308

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to a method of treating depression or anxiety in a mammal, including a human, by administering to the mammal a PDE IV inhibitor in combination with an antidepressant or an anxiolytic agent. It also relates to pharmaceutical compositions containing a pharmaceutically acceptable carrier, a PDE IV inhibitor and an anxiolytic agent or antidepressant.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 298680-25-8

(treatment for depression and anxiety by combination of a PDE IV inhibitor and an antidepressant or an anxiolytic agent)

RN 298680-25-8 USPATFULL

Me Me Me
$$CH_2-CH_2-NH-C-NH_2$$